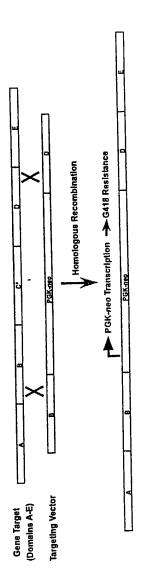


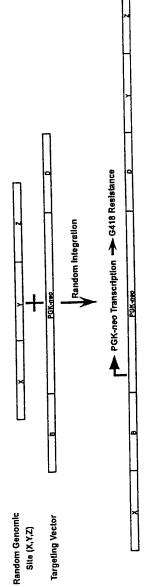
GENERATE KNOCK-OUT MOUSE FROM MUTANT CELL LINE

Homologous Recombination: G418 Resistance. Targeting Vector Flanked by "A" and "E"



Random Integration: G418 Resistance, Targeting Vector Flanked by "X" and "Y"

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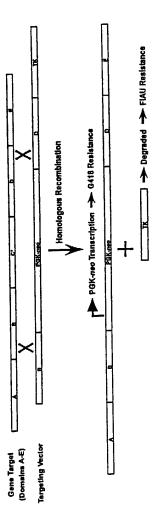


DISTINGUISH EVENTS BY SCREENING MOLECULARLY (PCR & SOUTHERN)

FIGURE 2







Random Integration: G418 Resistance + FIAU Sensitivity

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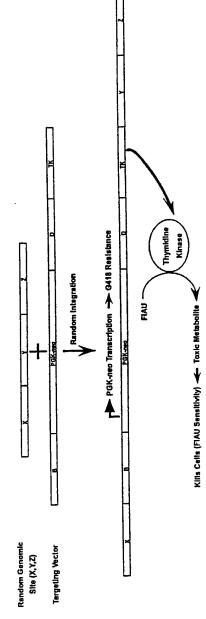


FIGURE 3





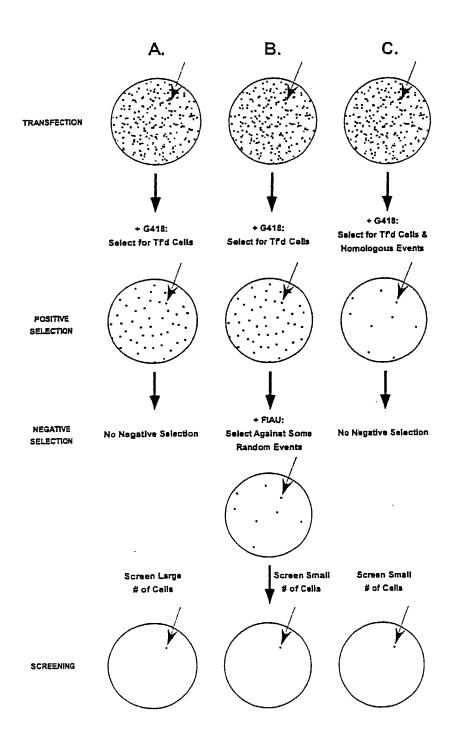
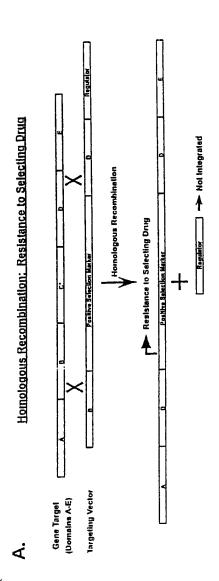
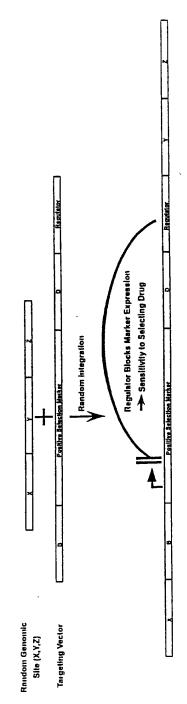


FIGURE 4





Random Integration: Sensitivity to Selecting Drug

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FIGURE 5

30.4

C3406:

GTTAACTACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGC <u>TCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCC</u> TTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGT GGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCGAAGAACGTTCTCCAATGATGAGCACTTTTAAAG TTCTGCTATGTGGCGCGGTATTATCCCGTGTTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTT GAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACAC TGCGGCCAACTTACTTTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTG CTCGGCCCTTCCGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAG ATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGT CCCAAAAACAGGAAGATTGTTATAAGCAAATATTTAAATTGTAAACGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAG CTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGCCCGAGATAGGGTTGAGTGTTGTTCCAGTTT GGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAAACCA TCACCCARATCRAGITITITGGGGTCGAGGTGCCGTARAGCACTARATCGGAACCCTARAGGGAGCCCCCGAITTAGAGCTTGACGGG <u> Aaagcgaacgtggcgagaaggaagggaagaaagcgaaaggagcggcgctagggcgctggcaagtgtagcggtcacgctgccctaac</u> CACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATC CCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAAT GCTTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACA TACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACC GGATAAGGCGCAGCGGTCGGGCTGAACGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTAC AGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGAGCGC ACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATG CTCGTCAGGGGGGGGGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGT TRATCGACATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCCATATATGGAGTTCCGCGTTACAT AACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCA <u>ATAGGGACTTTCCATTGACGTCAATGGGAGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTAC</u> GAGGGCCGGGCGGGGCGAGGCGAAAGGTGCGGCGGCAGCCAATCAGAGCGGCGCGCTCCGAAAGTTTCCTTTTATGGCGAGGCGGCG GAGCCGCAGCCATTGCCTTTTATGGTAATCGTGCGAGAGGGCGCAGGGACTTCCTTTGTCCCAAATCTGGCGGAGCCGAAATCTGGGAG GCGCCGCCCTTCCCCTTCTCCAGCCTCGGGGCTGCCGCAGGGGGACGGCTGCCTTCGGGGGGACGGGCAGGGCGGGGTTCGG CTTCTGGCGTGTGACCGGCGGCTCTAGAGCCTCTGCTAACCATGTTCATGCCTTCTTCTTTTTCCTACAGCTCCTGGGCAACGTGCTGG TTGTTGTGCTGTCTCATCATTTTGGCAAAGAATTCACCTGCCAGACATGCCAAAAAAGAGAAAAGGTCATGAAAACCAGTAACGTTA TTGCCACCTCCAGTCTGGCCCTGCACGCGCGTCGCAAATTGTCGCGGCGATTAAATCTCGCGCCGATCAACTGGGTGCCAGCGTGGTG GTGTCGATGGTAGAACGAAGCGGCGTCGAAGCCTGTAAAGCGGCGGTGCACAATCTTCTCGCGCAACGCGTCAGTGGGCTGATCATTAA CCATCAACAGTATTATTTTCTCCCATGAAGACGGTACGCGACTGGGCGTGGAGCATCTGGTCGCATTGGGTCACCAGCAAATCGCGCTG <u>GGAACGGGAAGGCGACTGGAGTGCCATGTCCGGTTTTCAACAAACCATGCAAATGCTGAATGAGGGCATCGTTCCCACTGCGATGCTGG</u> TTGCCAACGATCAGATGGCGCTGGGCGCAATGCGCGCCATTACCGAGTCCGGGCTGCGCGTTGGTGCGGATATCTCGGTAGTGGGATAC GACGATACCGAAGACAGCTCATGTTATATCCCGCCGTCAACCACCATCAAACAGGATTTTCGCCTGCTGGGGCAAACCAGCGTGGACCG CTTGCTGCAACTCTCTCAGGGCCAGGCGGTGAAGGGCAATCAGCTGTTGCCCGTCTCACTGGTGAAAAGAAAAACCACCTGGCGCCCA ATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGAA TTCACTCCTCAGGTGCAGGCTGCCTATCAGAAGGTGGTGGCTGGTGTGGCCAATGCCCTGGCTCACAAATACCACTGAGATCTTTTTCC TTACATGTTTTACTAGCCAGATTTTTCCTCCTCTCTGACTACTCCCAGTCATAGCTGTCCCTCTTCTCTTATGAAGATCCCTCGACCT GCAGCCCAGCCCAAGCTCGGGGCCAGGTCGGCCGAGCGATCGCGAGAATTCGGCTTAAGTGAGTCGTATTACGGACTGGCCGTCGTTTT <u>ACAACGTCGTGACTGGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAG</u> aggecegeaeegategeetteeeaaeagttgegeageetgaatggegaatggegttegettggtaataaageeggtteggegget 

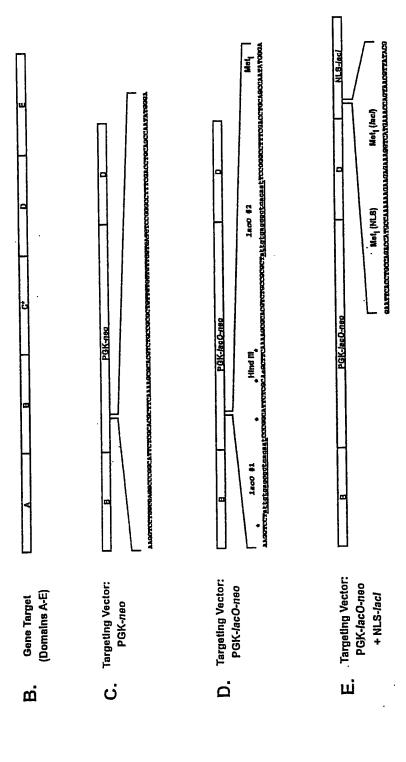
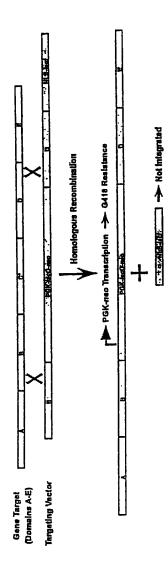


FIGURE 6 B-E





Homologous Recombination: G418 Resistance



Random Integration: G418 Sensitivity

B.

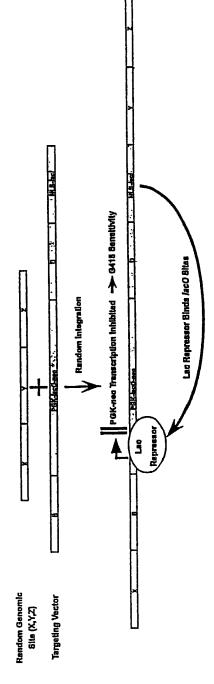
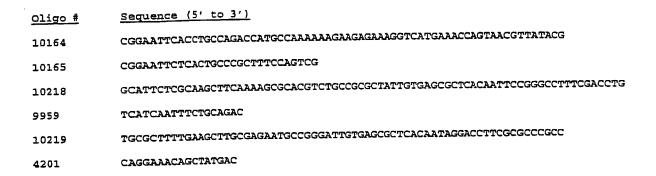


FIGURE 7





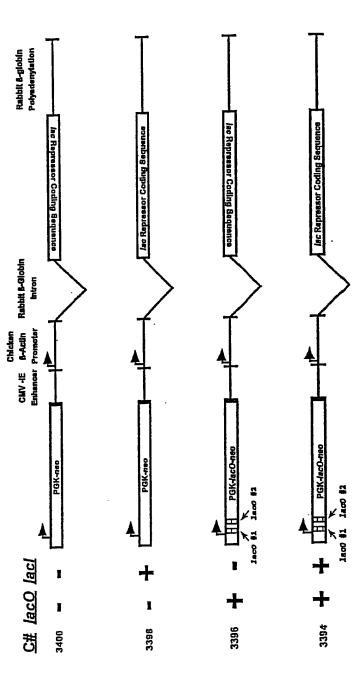
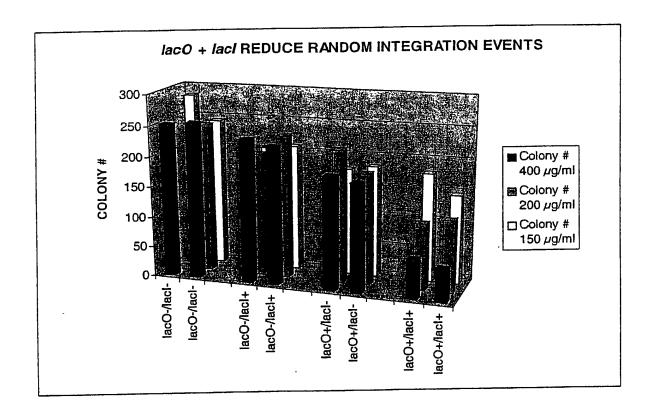


FIGURE 9





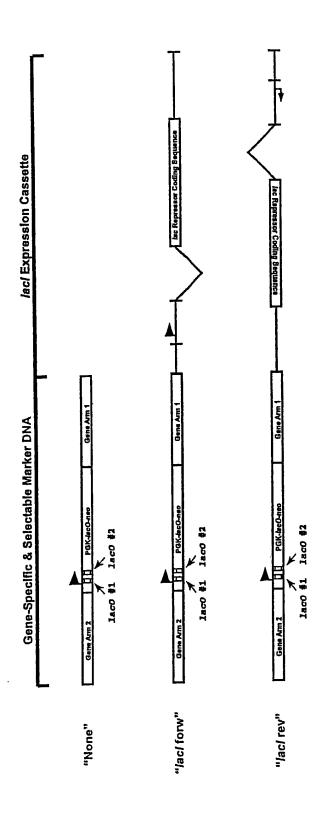
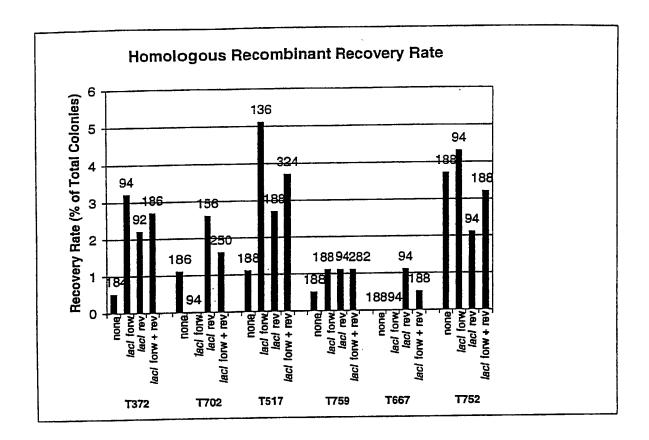
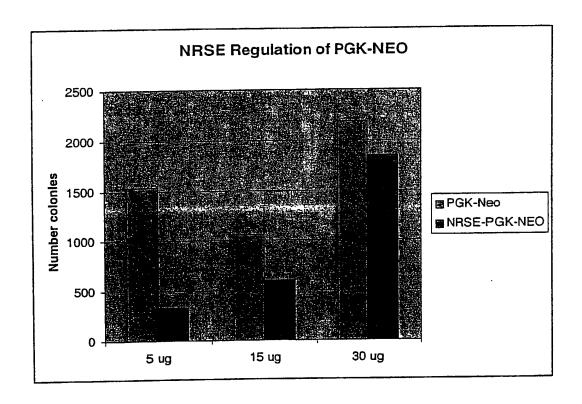


FIGURE 11







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16/16

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